

Topic 5 – Diabetes, Lipids, metabolism – A

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0396

Prebiotics supplementation improves the endothelial dysfunction induced by a nutritional deficiency in n-3 polyunsaturated fatty acids (PUFA)

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Nutritional disorders are associated with a high risk of developing cardiovascular diseases, endothelial dysfunction being an early key marker. We have demonstrated that metabolic alterations induced by a nutritional depletion in n-3 PUFA are improved by a supplementation in prebiotics (non-digestible fructans). The present work focusses on the impact of prebiotics on the endothelial dysfunction induced by the n-3 PUFA depletion in ApoE^{-/-} mice model.

C57Bl/6J (WT) and ApoE^{-/-} (KO) mice were fed a n-3 PUFA depleted-diet (DEF) for 12 weeks. For the last fifteen days, mice were or not supplemented with prebiotics (PRE). The vascular morphology and function were evaluated in first, second and third order mesenteric arteries by histology and wire myograph.

Micro-arteries from KO DEF PRE mice develop an increased basal tone and present a larger vessel diameter, compared to vessels from non-supplemented mice. The PRE supplementation in KO DEF mice leads to an increased media thickness in first order mesenteric arteries, this is even higher in the second order branch, in comparison to non-supplemented mice. KO DEF PRE micro-arteries contract significantly more in response to a KCl challenge than vessels from non-supplemented mice. As expected micro-arteries from KO DEF mice present an endothelial dysfunction after 12 weeks of n-3 PUFA depletion with a significant decrease of endothelial-dependent relaxation in comparison to WT DEF arteries. The PRE supplementation is able to improve the endothelial function by restoring the endothelial-dependent relaxation in arteries from KO DEF mice.

We point out fructan-type prebiotics as a potential therapeutic tool in endothelial dysfunction. Our results argue in favor of an outward muscular remodeling in mesenteric arteries, leading to an increased blood flow and a better vascular reactivity. The results on endothelial function evoke an important implication of the nitric oxide pathway in this phenomenon.

0061

Exercise training impaired energy metabolism and function of the type 2 diabetic Goto-Kakizaki (GK) rat heart during ischaemia-reperfusion injury

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Background: Informations about the effects of exercise training on diabetes-induced myocardial dysfunctions are lacking. Consequently, we investigated the effect of exercise training on the sensitivity of the type 2 diabetic Goto-Kakizaki (GK) rat heart to ischaemia-reperfusion injury by using a multiparametric approach combining 31P magnetic resonance spectroscopy (MRS) with simultaneous measurement of contractile function and biochemical assays.

Materials and Methods: 8-month-old male GK rat (n=11, trained GK) rats ran 60 min on a treadmill 5 days/week at a speed of 20 m/min for 7 weeks and compared with age-matched male Control (n=6) and untrained GK (n=11) rats. Then, isolated rat hearts were perfused with a physiological buffer containing 0.4 mM palmitate, for 24 min before switching to 1.2mM palmitate during

32min low-flow (0.5 ml/min-1.g wet wt-1) ischaemia. Next, flow was restored with 0.4 mM palmitate buffer for 32 minutes. High energy compounds and intracellular pH were followed using 31P MRS with simultaneous measurement of contractile function. Total adenine nucleotides (TAN) and energy charge (EC) were determined in freeze-clamped tissues by H.P.L.C.

Results: Heart to body weight ratios were significantly higher in both untrained and trained diabetic groups (p<0.02) versus Control. During reperfusion, rate pressure product and recoveries of PCr and ATP were significantly lower (p<0.05) in trained GK versus untrained GK and Control rat hearts. TAN and EC were significantly decreased in trained GK compared with Control (p=0.0052 and p=0.0156) and untrained GK (p=0.0024 and p=0.0005) rat hearts.

Conclusion: The intensity of exercise training exacerbated the sensitivity of the type 2 diabetic 8-month-old Goto-Kakizaki rat to myocardial ischaemia-reperfusion by impairing energy metabolism and myocardial performance. Other exercise protocols and/or therapeutic approaches need to be explored to limit myocardial ischaemia-reperfusion injury in type 2 diabetes.

0205

Exercise training prevents microvascular dysfunction in a rat model of diet-induced metabolic syndrome

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Introduction: Metabolic syndrome (MetS) is associated with increased risk of cardiovascular disease (CVD). One important key feature underlying the pathophysiology of CVD is microvascular dysfunction. Although, exercise training is a well recognized strategy to reduce cardiovascular and metabolic disorders, the impact on MetS induced microvascular dysfunction is poorly described and the underlying mechanisms remain unknown. Thus, the aim of this work was to evaluate the effect of physical activity on microvascular reactivity in a rat model of MetS.

Methods: Rats were fed with standard (Ctrl group) or high-fat and sucrose diet (HFS group) for 14 weeks. After 6 weeks, HFS rats were randomly assigned into 2 groups: sedentary (HFS) and trained group (HFS-Ex). In vivo endothelial function was evaluated by skin Laser Doppler technique associated to transcutaneous iontophoresis at 06 and 14 weeks. Body weight, metabolic parameters and blood pressure were also measured.

Results: High-fat and sucrose diet induced a significant body weight raise accompanied by the increase of serum level of glucose, triglycerides, HDL and LDL-cholesterol. All of these parameters were restored after 4 weeks of exercise training in HFS-Ex group. In addition, skin endothelium-dependent dilation, which was decreased in HFS compared to Ctrl, was prevented by exercise training. This result could be explained by increased level of eNOS expression and phosphorylation on its activation site (ser1177).

Conclusion: These results mainly suggest that an exercise training strategy, which is able to partially correct metabolic disorders in a model of MetS in rats, also prevents in vivo microvascular dysfunction.

0158

Effect of polyphenols of olive oil, hydroxytyrosol and its glucuronides on the vascular reactivity in a type 2 diabetes context

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Hydroxytyrosol (HT) and Resveratrol (RES) are recognized as strong antioxidant polyphenolic compound. While RES antioxidative mechanisms are well known, those of HT are controversial because of its low intestinal absorp-